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EXAMINER	
KUBELIK, ANNE R 13	
ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 03/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/887,038	KAPLAN ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,8-11,13-16,19-23 and 26-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,8-11,13-16,19-23 and 26-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 November 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The specification has been amended, claims 5, 7, 12, 17-18 and 24-25 have been cancelled and claims 1-2, 6, 8-20, 13, 16, 19-23 and 26-30 have been amended, as requested in Paper No. 12, filed 29 November 2002. Claims 1-4, 6, 8-11, 13-16, 19-23 and 26-30 are pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The drawings are objected to for the reasons indicated on the accompanying form PTO 948. Corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance. See 37 CFR 1.85(a) and MPEP 608.02(b).

Response to Amendment

4. The rejection of claims 1-30 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,320,101 is WITHDRAWN in light of the filing of a terminal disclaimer over that patent.

5. The rejection of claims 16-20 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is WITHDRAWN in light of amendments to the claims to claim a nucleic acid construct.

6. The rejection of claims 16-20 and 22 under 35 U.S.C. 102(b) as being anticipated by Bonfil et al (1996, GenBank Accession No. U62616) is WITHDRAWN in light of amendments to the claims to claim a nucleic acid construct comprising a plant promoter.

7. The rejection of claims 23-25 and 28-29 under 35 U.S.C. 102(b) as being anticipated by Gordon-Kamm et al (1990, Plant Cell 2:603-618) is WITHDRAWN as Gordon-Kamm et al does not teach transformation with a nucleic acid encoding a protein with carbon fixation activity.

Claim Objections

8. Claim 3 remains objected to because "Agrobaterium" in line 3 is misspelled.

Claim Rejections - 35 USC § 112

9. Claims 1-4, 6-11, 13-16, 19-23 and 26-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Neither the instant specification nor the originally filed claims appear to provide support for the phrases "a polynucleotide capable of hybridizing under high stringency conditions" and "wherein said polynucleotide encodes a polypeptide having an inorganic carbon fixation activity". Thus, such phrases constitute NEW MATTER. In response to this rejection, Applicant is required to point to support for the phrases or to cancel the new matter.

10. Claims 1-4, 6-11, 13-16, 19-23 and 26-30 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids of SEQ ID NO:2, a method of enhancing inorganic carbon fixation in a plant by transformation with a nucleic acid of SEQ ID NO:2, and plants so obtained, does not reasonably provide enablement for nucleic acids that encode a protein that is 90% homologous to the polypeptide of SEQ ID NO:3 or that

hybridize to SEQ ID NO:2, a method of enhancing inorganic carbon fixation in a plant by transformation with those nucleic acids, and plants so obtained. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is modified from the rejection set forth in the Office action mailed 28 May 2002, as applied to claims 1-30, due to amendment of the claims. Applicant's arguments filed 29 November 2002 have been fully considered but they are not persuasive.

The claims are broadly drawn to a multitude of DNA molecules from a multitude of sources that hybridize to SEQ ID NO:2 wherein the nucleic acid encodes a protein with inorganic carbon fixation activity and wherein the nucleic acid is operably linked to a plant promoter. The claims are also drawn to a method of enhancing carbon fixation in a photosynthetic organism through transformation with those nucleic acids, and photosynthetic organisms so produced.

The instant specification, however, only provides guidance for cloning the IL-2 gene (SEQ ID NO:2) from *Synechococcus* PCC7942 (pg 44-46), methods of transformation with this nucleic acid (pg 26-39) to produce plants with increased carbon fixation rates (pg 54-56), and methods of measuring photosynthesis and carbon uptake in *Synechococcus* PCC7942 (pg 41-42).

The specification fails to provide guidance for a nucleic acid that hybridizes to SEQ ID NO:2 and that encodes a protein with inorganic carbon fixation activity, methods of using it, and plants thereby obtained.

Identifying nucleic acids functionally related to a given nucleic acids is highly unpredictable. For example, creating variants of a gene by making "conservative" substitutions

(*e.g.*, substituting one polar amino acid for another, or one acidic one for another) is not predictable. Lazar et al (*supra*) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). The nucleic acids encoding all these mutated proteins would hybridize under high stringency to the nucleic acids encoding the original protein.

A great many proteins have "inorganic carbon fixation activity", including those required for leaf structure and development (Čatský et al, Handbook of Photosynthesis, 1997, Pessarakli, M., ed., Dekker, New York, N. Y., pg 633-660, see 635-641), and metal transport (Pakrasi et al, 2001, In *Regulation of Photosynthesis*, Aro et al, eds., pg 253-264, see *e.g.* Table 1), as well as a variety of enzymes involved in varying aspects of the carbon cycles (Čatský et al, pg 641-643). Assaying the claimed nucleic acid to determine if it encodes a nucleic acid with any one of these multitudes of enzymatic activities would require undue experimentation.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate the claimed nucleic acids. Making all possible single amino acid substitutions in an 467 amino acid long protein like that encoded by SEQ ID NO:1 would require making and analyzing 19^{467} nucleic acids; these proteins would have 99.8% identity to SEQ ID NO:3. Because nucleic acids

encoding proteins with 90% identity to SEQ ID NO:3 or nucleic acids that hybridize to SEQ ID NO:2 would encode proteins with at least 46 amino acid substitutions, many more than 19^{467} nucleic acids would need to be made and analyzed.

As the specification does not describe the transformation of any plant with a nucleic acid that hybridizes to SEQ ID NO:2, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with increased carbon fixation activity, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

Applicant urges that SEQ ID NO:3 encodes a bicarbonate transporter because transformation of a plant with the nucleic acid increased concentration of CO_2. Applicant believes the claims have been amended to expedite prosecution. Applicant urges that polynucleotides are well-known entities and cites a number of patents that claim a nucleic cid that hybridize under high stringency conditions to a particular SEQ ID NO:. Applicant urges that methods of stringent hybridization are standard techniques and cites Duester et al to state that many families of genes encoding functionally equivalent polypeptides have 85% or even lower homology. Applicant urges that the claims are restricted to photosynthetic plants, overcoming objections to lack of guidance for methods of transformation of other photosynthetic organisms. Applicant urges that isolation of a gene encoding sequences homologous to and having the same

function as a defined sequence is well-known in the art; Applicant cites a number of patents and a web site to support this (response pg 8-15).

This is not found persuasive because, as discussed above, a great many proteins play a role in inorganic carbon fixation. Assaying the proteins encoded by nucleic acids that hybridize to SEQ ID NO:2 to determine if they have one of the multitude of possible inorganic carbon fixation activities would require undue experimentation.

Duester et al, the patents and the information on the web site could not be considered because they were not sent.

11. Claims 1-4, 6-11, 13-16, 19-23 and 26-30 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is modified from the rejection set forth in the Office action mailed 28 May 2002, as applied to claims 1-30, due to amendment of the claims. Applicant's arguments filed 29 November 2002 have been fully considered but they are not persuasive.

The claims are broadly drawn to a multitude of DNA molecules that hybridize to SEQ ID NO:2, or that comprise any variation of a portion of any size of SEQ ID NO:2, wherein the DNA molecules are operably linked to a plant promoter and wherein the DNA molecules encode a protein with an inorganic carbon fixation activity, methods of using them to obtain a photosynthetic plant with enhanced inorganic carbon fixation, and plants thereby obtained. In contrast, the specification only describe a nucleic acid from *Synechococcus* that comprises SEQ ID NO:2. Applicant does not describe other DNA molecules encompassed by the claims, and the

structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

A great many proteins of very different enzymatic activity play a role in inorganic carbon fixation, as discussed above, and can thus be said to have an inorganic carbon fixation activity. Applicant has not described nucleic acids encoding all these proteins.

Hence, Applicant has not, in fact, described DNA molecules that encode a protein with inorganic carbon fixation activity, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed, Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

Applicant urges that polynucleotides are well-known entities and cites a number of patents that claim a nucleic acid that hybridize under high stringency conditions to a particular SEQ ID NO:. Applicant urges that methods of stringent hybridization are standard techniques and cites Duester et al to state that many families of genes encoding functionally equivalent polypeptides have 85% or even lower homology (response pg 8-15).

This is not found persuasive because a complete description of the claimed nucleic acid, and plants comprising those nucleic acids and methods of using them, requires a specific description of the function of the protein encoded by the nucleic acid.

Duester et al and the patents could not be considered because they were not sent.

12. Claims 1-4, 6, 8-11, 13-16, 19-23 and 26-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is modified from the rejection set forth in the Office action mailed 28 May 2002, as applied to claims 1-15, 17-21 and 24, due to amendment of the claims. Applicant's arguments filed 29 November 2002 have been fully considered but they are not persuasive.

Applicant urges that claims have been amended to address these issues (response pg 15-16). This is not found persuasive because the following rejections remain or are new:

Claim 15 remains indefinite in its recitation of "further includes". It is unclear if "includes" is intended to be open or closed. If open language is intended, the word should be replaced with "comprises." Additionally, the polynucleotide of part (i) of Claim 1 does not "include" anything so the polynucleotide cannot "further include" something.

Claims 6 and 19 remain indefinite in their recitation of the word "homologous". It is not clear if by this word, Applicant intends the sequences be 90% identical to or 90% related in some other unspecified manner to SEQ ID NO:3.

Claims 6 and 19 lack antecedent basis for the limitation "the Blast software" in line 3.

Claim 14 remains indefinite in its recitation of the phrase "independently selected" in parts (i), (ii), and (iii). It is unclear from what the selection of the promoter must be independent. Deletion of "independently" would obviate the rejection.

Claims 15 and 22 remain indefinite in their recitation of the word "derived" in lines 8-10 and 6-7, respectively. It is not clear what has been done to those virus, plasmids and transposable element sequences to make them "derived" and how they differ from the original viruses, plasmids and transposable elements.

The following rejections are new, due to amendment of the claims:

Claims 1 and 16 are indefinite in the recitation of "high stringency conditions" in parts (i) and (a), respectively. It is not clear what conditions are considered high stringency.

Claims 1 and 16 are indefinite in the recitation of "inorganic carbon fixation activity" in parts (i) and (a), respectively. It is unclear what inorganic carbon fixation activity is - is it just the activity of Rubisco, which is the enzyme ultimately responsible to fixing carbon dioxide, or does the phrase refer to any enzymatic activity that plays any sort of role in any aspect of inorganic carbon fixation, including the proteins responsible for transcription and translation of Rubisco? The metes and bounds of the claim are unclear.

Claim 16 is indefinite in its recitation of "promoter being for directing". Does Applicant intend that the promoter be one that directs transcription or is something else intended?

Claim Rejections - 35 USC § 102

13. Claims 1-4, 8-9, 13-16, 20-23, 26-27 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Ko et al (US Patent 6,011,198, filed December, 1996). The rejection is modified from the rejection set forth in the Office action mailed 28 May 2002, as applied to claims 23-27 and 30, due to amendment of the claims. Applicant's arguments filed 29 November 2002 have been fully considered but they are not persuasive.

Ko et al teach tobacco plants transformed via *Agrobacteria*-mediated methods with a nucleic acid encoding the chlorophyll a/b binding protein, wherein the nucleic acid is operably linked to the constitutive CaMV 35S promoter, a transit peptide encoding sequence, and the Cab termination signal, and a method of making them plants (column 25, line 45, to column 27, line 16). These plants have a rate of photosynthesis 37% higher than that of non-transgenic tobacco plants (column 29, line 25, to column 30, line 67). The chlorophyll a/b binding protein has an inorganic carbon fixation activity, because it is responsible for light harvesting in inorganic carbon fixation. The nucleic acid would hybridize under unspecified "high stringency conditions" to SEQ ID NO:2. Ko et al also teach transformation via electroporation, particle bombardment, and viruses (column 12, lines 35-49), and transformation by these methods would inherently be transient in at least some cells.

Applicant urges that the claims have been amended to exclude naturally occurring plants (response pg 17-18). This is not found persuasive because the claims have been amended to claim plants transformed with a nucleic acid encoding a protein with inorganic carbon fixation activity and methods of making those plants. The nucleic acid taught by Ko et al encodes a

protein with such an activity and the nucleic acid would hybridize under some definitions of high stringency conditions.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 1-4, 8-11, 13-16, 20-23 and 26- 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ko et al (US Patent 6,011,198, filed December, 1996) in view of Gordon-Kamm et al (1990, Plant Cell 2:603-618).

The claims are broadly drawn to a multitude of DNA molecules from a multitude of sources that hybridize to SEQ ID NO:2 wherein the nucleic acid encodes a protein with inorganic carbon fixation activity and wherein the nucleic acid is operably linked to a plant promoter. The claims are also drawn to a method of enhancing carbon fixation in a plant through transformation with those nucleic acids, and plants, including maize plants, so produced.

The teachings of Ko et al are discussed above. Ko et al do not disclose corn plants transformed with the nucleic acid.

Gordon-Kamm et al teach transformation of maize plants (pg 607).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of producing plants with increased inorganic carbon fixation by transformation with a nucleic acid encoding the chlorophyll a/b binding protein, as taught by Ko

et al, to transform the nucleic acid into maize as described in Gordon-Kamm et al. One of ordinary skill in the art would have been motivated to do so because of the economic importance of maize.

16. Claims 6 and 19 are free of the prior art are free of the prior art, given the failure of the prior art to teach or suggest plant transformation with a nucleic acid that encodes a protein with 90% identity to SEQ ID NO:3, wherein the nucleic acid encodes a protein with inorganic carbon fixation activity and wherein the nucleic acid is operably linked to a plant promoter.

Conclusion

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
February 21, 2003

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